

BINARY ENCODED SEQUENCE TAGS

ABSTRACT OF THE DISCLOSURE

Disclosed is a method for the comprehensive analysis of nucleic acid samples and a detector composition for use in the method. The method, referred to as Binary Encoded Sequence Tags (BEST), involves generation of a set of nucleic acid fragments; adding an adaptor to the ends containing recognition site for cleavage at a site offset from the recognition site; cleaving the fragment to generate fragments having a plurality sticky ends; indexing of the fragments into sets based on the sequence of sticky ends. The fragments are indexed by adding an offset adaptor to newly generated ends. A different adaptor will be coupled to each different sticky end. The resulting fragments—which will have defined ends, be of equal lengths (in preferred embodiment), and a central sequence derived from the source nucleic acid molecule—are binary sequence tags. The binary sequence tags can be used and further analyzed in numerous ways. For example, the binary sequence tags can be captured by hybridization and coupling, preferably by ligation, to a probe. The probe is preferably immobilized in an array or on sortable beads. One form of the BEST method, referred to as modification assisted analysis of binary sequence tags (MAABST), assesses modification of sequences in nucleic acid molecules by detecting differential cleavage based on the presence or absence of modification in the molecules.